UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/759,561	01/15/2004	David M. Weiner	12560-016-999	8108

20583 7590 01/06/2009

JONES DAY
222 EAST 41ST ST
NEW YORK, NY 10017

EXAMINER	
KIM, JENNIFER M	

ART UNIT	PAPER NUMBER
1617	

MAIL DATE	DELIVERY MODE
01/06/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/759,561	WEINER ET AL.	
	Examiner	Art Unit	
	JENNIFER MYONG M. KIM	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10/14/2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-8,48 and 90-106* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8,48 and 90-106* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *10/14/2008*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicants' submission filed on October 14, 2008 has been entered.

Response to Arguments

Applicants' arguments filed October 14, 2008 have been fully considered but they are not persuasive. Applicants argue that Drug News 2001 does not disclose the chemical structure of the compound of Formula (I) of claim 48, nor does it provide any information about the structure of the compound. This is not found to be persuasive because Drug News 2001 identifies the compound by its known name, i.e. ACP-103. It is also admit by the Applicants on their provisional Applications 60/441,406 and 60/479,346 that ACP 103 is N-(1-methylproderidin-4-yl)-N-(4-flourophenylmethyl)-N'-(4-(2-methylpropyloxy)phenylmethyl)carbamide (2R,3R)-dihydroxybutanedioate (2:1). Therefore, this teaching of Drug News 2001 fully met the limitations of the claim 48. Applicants argue that Andersson teaches a broad genus of compounds that encompasses the compound of Formula (I), however, the compound is not specifically

disclosed in Andersson. Therefore, the Examiner has not demonstrated how one of ordinary skill in the art would be motivated to select the specific variables from the genus of Andersson in order to arrive at the compound of the instant claims. This is not found to be persuasive because it is clear from the teaching of R&D Focus Drug News teaches that ACP-103 comprising formula I (N-methylpiperidin-4-yl)-N-(4-flurophenylmethyl)-N'-(4-(2-methylpropyloxy)phenylmethyl)carbamide) with its acceptable pharmaceutical salt set forth in claim 48 is a selective 5HT2A inverse agonist and has a potential antipsychotic agent with an improved side-effect profile while Anderson et al. teaches the effectiveness of the genus of compound having same chemical motif for the treatment of various neurological disorders. A genus does not always anticipate a claim to species within the genus. However, the species is clearly named in the Drug News reference as having the useful therapeutic effect. Therefore, the comprehensiveness of the genus in Anderson et al. does not negate the fact the compound claimed having such useful therapeutic effect as taught by Drug News reference. Applicants argue that Goodman & Gilman does not cure the defects of Drug News and Andersson. This is not found persuasive because the Goodman & Gilman reference was cited to show the obviousness of combining components that are taught to have the same therapeutic effects. Applicants argue that the Applicants have demonstrated unexpected results to show that the compound and salts of the instant claims possess unexpected properties sufficient to rebut a prima facie case of obviousness. This is not found to be persuasive because the Bonhaus Declaration has been carefully reviewed and considered. However, it is not persuasive because the

data comparing about 100 compounds from Andersson with the tartrate and hydrochloride salt of the compound of Formula I. However, Applicants are reminded that when relying on comparative testing, the applicants are under a duty to compare his claimed invention with the closest prior art (i.e. R&D Drug News, compound ACP-103). See, In re Burckel, 592 F.2d 1175, 201 USPQ 67 (CCPA 1979); In re Merchant, 575 F.2d 865, 197 USPQ 785 (CCPA 1978); Ex parte Beck, 9 USPQ 2d 2000, 2002 (Bd. Pat. App. & Int. 1987) ("comparative evidence, to be effective, must compare the claimed subject matter with the closest prior art"); Ex parte Meyer, 6 USPQ2d 1966, 1968 (Bd. Pat. App. & Int. 1988) ("An applicant relying upon a comparative showing to rebut a prima facie case of obviousness must compare his claimed invention with the closet prior art.").

Applicants' data does not indicate how the hydrochloride and tartrate form of the instant compound set forth in claim 48 achieves better stability compare the active compound of R&D Drug News (AP-103), and thus, it does not appear that Applicants have compared the claimed composition and compounds with that of the closest prior art. Thus, the claims fail to patentably distinguish over the state of the art as represented by the cited references.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 48 is rejected under 35 U.S.C. 102(b) as being anticipated by R&D Focus Drug News (12 Nov. 2001) of record evidenced by Applicants' admission.

R&D Focus Drug News teaches that ACP-103 comprising formula I (N-methylpiperidin-4-yl)-N-(4-fluruphenylmethyl)-N'-(4-(2-methylpropyloxy)phenylmethyl)carbamide) with its acceptable pharmaceutical salt set forth in claim 48 is a selective 5HT2A inverse agonist and has a potential antipsychotic agent with an improved side-effect profile. R&D Focus Drug News teaches that ACP 103 was found to be orally bioavailable with a high efficacy, in animal models of psychosis.

Applicants admit on their provisional Applications 60/441,406 and 60/479,346 that ACP 103 is N-(1-methylproderidin-4-yl)-N-(4-flourophenylmethyl)-N'-(4-(2-methylpropyloxy)phenylmethyl)carbamide (2R,3R)-dihydroxybutanedioate (2:1).

Claim Rejections - 35 USC § 103

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 1-8 and 90-106 are rejected under 35 U.S.C. 103(a) as being unpatentable over R&D Focus Drug News (12 Nov. 2001) in view of Anderson et al. (WO0166521-IDS 01/18/2005) of record and further in view of and further in view of Goodman and Gilman's The Pharmacological Basis of Therapeutics, 7th edition, pages 340-343 and 403-404 of record.

R&D Focus Drug News teaches that ACP 103 also known as is N-(1-methylproderidin-4-yl)-N-(4-flourophenylmethyl)-N'-(4-(2-methylpropyloxy)phenylmethyl)carbamide (2R,3R)-dihydroxybutanedioate (2:1) is a selective 5HT2A inverse agonist and has a potential antipsychotic agent with an improved side-effect profile. R&D Focus Drug News teaches that ACP 103 was found to be orally bioavailable with a high efficacy, in animal models of psychosis.

R&D Focus Drug News does not expressly teach a pharmaceutically acceptable carrier and an additional agents, dosage amounts and formulations including tablets and capsules and the specified salts including hydrochloride salt, tartrate salt and its free form.

Anderson et al. teach that the compounds broadly including the active agent, N-(1-methylproderidin-4-yl)-N-(4-flourophenylmethyl)-N'-(4-(2-methylpropyloxy)phenylmethyl)carbamide can be formulated with pharmaceutically acceptable insert carrier such as ethanol, glycerol, water and the like. Anderson et al. teach that when desired or necessary, suitable binders, lubricants, disintegrating agents, flavoring agents and disintegrating agents can be also incorporated into the mixture comprising the compound. (page 29, lines 27-30). Anderson et al. teach on

pages 9-12, compounds of formula I that broadly encompasses the currently disclosed formula I and suitable pharmaceutically acceptable salts such including **hydrochloride and tartrate**. (Page 27, line30-page 28 line 14). On page 32 lines 12-25, Anderson et al. disclose the co-administration of the compounds of formula I with either another compound of formula I or another active agent. One page 6, Anderson et al. disclose that the compounds of formula I are useful for treating variety of diseases and disorders including **schizophrenia, depression, anxiety, sleep disorder**, etc. Anderson et al. disclose that the formula I, avoid the adverse side effects such as dyskinesia, tremor and dystonic reactions. (page 4, lines 28-33, page 3, lines 9-10). The therapeutic applications: **neurodegenerative disease, psychosis, schizophrenia, depression** and affective disorders are explicitly mentioned to be treatable with compounds of Anderson et al.

Goodman and Gilman's teaches, on page 340-343 teach, benzodiazepines useful in the treatment of anxiety, muscle relaxation and anticonvulsive therapy. On page 342, clonazepam is taught as a particularly good muscle relaxant. On page 343, it is disclosed that benzodiazepines increase the net total sleep time, making them unsuitable as agents for sleep disorders. Goodman and Gilman's teaches, on page 403-404, several anti-psychotic agents including Thorazine, Mellaril, Haldol, etc.

It would have been obvious to one of ordinary skill in the art to modify the teaching of R&D Focus Drug News and formulate a pharmaceutical composition comprising the active agent, N-(1-methylproderidin-4-yl)-N-(4-flourophenylmethyl)-N'-(4-(2-methylpropyloxy)phenylmethyl)carbamide with its pharmaceutically acceptable salts

such as hydrochloride and tartrate for treatment of psychosis because R&D Focus Drug News teaches the active agent with its pharmaceutical salt such as dihydroxybutanedioate, was found to be orally bioavailable with a high efficacy, in animal models of psychosis and because Anderson teaches that the general compounds including the active agent set forth in claim 1 can be combined with a pharmaceutically acceptable carrier and pharmaceutically acceptable salts such as hydrochloride and tartrate for oral administration. One would have been motivated to make such a modification in order to achieve an expected antipsychotic benefit of the active agent in oral formulation with a benefit of having an improved side-effect profile. There is a reasonable expectation of successfully formulating active agent with a pharmaceutically acceptable salts such as hydrochloride and tartrate as an antipsychotic agent because there is a clear teaching from R&D Focus Drug News that the active agent with a pharmaceutical salt (i.e. dihydroxybutanedioate) was found to be orally bioavailable with a high efficacy, in animal models of psychosis and because Anderson et al. teach that these pharmaceutically acceptable salts (i.e. hydrochloride and tartrate) can be formulated with the active agent. With respect to incorporation of additional agents set forth in claim 3-8 are obvious because Anderson et al. disclose that coadministration of the compounds of formula I with other active agents and that the compound formula I is useful for the treatment of psychosis and related disorders such as neurodegenerative disease, psychosis, schizophrenia, depression and affective disorders and dyskinesia, tremor and dystonic reactions as taught by Anderson et al. It is noted that Goodman and Gilman teaches the additional agents are also useful for the

treatment of various conditions including psychosis, anxiety, sleep disorder and conditions related to psychosis. The motivation for combining the components flows from their individually known common utility (see In re Kerkhoven, 205 USPQ 1069(CCPPA 1980)). Thus, the claims fail to patentably distinguish over the state of the art as represented by the cited references.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-8, 48 and 90-106 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-3 and 5-7 of copending Application No. 11/134,769. Although the conflicting claims are not identical, they are not patentably distinct from each other because they

encompasses the same subject matter constitute with the same active agent. As such, the claims of the instant Application and the claims in the copending Application would have been obvious variations of the other to one of ordinary skill in the art.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 1-8, 48 and 90-106 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 16-18 of copending Application No. 11/416,855. Although the conflicting claims are not identical, they are not patentably distinct from each other because they encompasses the same subject matter constitute with the same active agent. As such, the claims of the instant Application and the claims in the copending Application would have been obvious variations of the other to one of ordinary skill in the art.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 1-8, 48 and 90-106 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 2 and 4-6 of copending Application No. 10/850/819. Although the conflicting claims are not identical, they are not patentably distinct from each other because they encompasses the same subject matter constitute with the same active agent. As such,

the claims of the instant Application and the claims in the copending Application would have been obvious variations of the other to one of ordinary skill in the art.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Inventorship

In view of the papers filed July 13, 2007, it has been found that this nonprovisional application, as filed, through error and without deceptive intent, improperly set forth the inventorship, and accordingly, this application has been corrected in compliance with 37 CFR 1.48(a).

The inventorship of this application has been changed by addition of:

Norman Nash

San Diego, CA

The application will be forwarded to the Office of Initial Patent Examination (OIPE) for issuance of a corrected filing receipt, and correction of Office records to reflect the inventorship as corrected.

Communication

Any inquiry concerning this communication or earlier communications from the examiner should be directed to JENNIFER M. KIM whose telephone number is (571)272-0628. The examiner can normally be reached on Monday through Friday 6:30 am to 3 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreenivasan Padmanabhan can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Jennifer Kim/
Primary Examiner, Art Unit 1617

Jmk
December 29, 2008